

FORM PTO-1083

COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, VA 22313-1450



Docket No.: 287.1006US

Date: August 10, 2005

In re application of: Ralph A. HEASLEY, et al.  
Serial No.: 10/631,371  
Filed: July 31, 2003  
For: TRANEXAMIC ACID FORMULATIONS WITH REDUCED ADVERSE EFFECTS

Sir:

Transmitted herewith is a **Supplemental Information Disclosure Statement** in the above-identified application.

- ☐ Small entity status of this application under 37 C.F.R. 1.9 and 1.27 has been established by a verified statement previously submitted.
- ☐ A verified statement to establish small entity status under 37 C.F.R. 1.9 and 1.27 is enclosed.
- ☒ No fee for additional claims is required.
- ☐ A filing fee for additional claims calculated as shown below, is required:

- ☒ Also transmitted herewith are:
  - ☐ Petition for extension under 37 C.F.R. 1.136 (in duplicate)
  - ☒ Other: **Form PTO-1449; copies of cited references; Exhibit A and Exhibit B**

- ☐ Check(s) in the amount of **\$00.00** is/are attached to cover:
  - ☐ Filing fee for additional claims under 37 C.F.R. 1.16
  - ☐ Petition fee for extension under 37 C.F.R. 1.136
  - ☐ Other:

- ☒ The Assistant Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 50-0552.
  - ☒ Any filing fee under 37 C.F.R. 1.16 for the presentation of additional claims which are not paid by check submitted herewith.
  - ☒ Any patent application processing fees under 37 C.F.R. 1.17.
  - ☒ Any petition fees for extension under 37 C.F.R. 1.136 which are not paid by check submitted herewith, and it is hereby requested that this be a petition for an automatic extension of time under 37 CFR 1.136.

  
David G. Knasiak, Reg. No. 45,991  
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I hereby certify that this correspondence and/or documents referred to as attached therein and/or fee are being deposited with sufficient postage to the United States Postal Service as "first class mail" in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on August 10, 2005.

DAVIDSON, DAVIDSON & KAPPEL, LLC

BY: 

BEST AVAILABLE COPY



## UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 10/631,371  
Applicant : Ralph A. Heasley, et al.  
Filed : July 31, 2003  
TC/AU : 1615  
Examiner : Not Yet Known  
Docket No. : 287.1006  
Customer No. : 23280  
Title : **TRANEXAMIC ACID FORMULATIONS  
WITH REDUCED ADVERSE EFFECTS**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

August 10, 2005

**SUPPLEMENTAL INFORMATION DISCLOSURE**  
**STATEMENT UNDER 37 C.F.R. § 1.56**

Sir:

In accordance with the provisions of 37 C.F.R. § 1.97, Applicants hereby make of record the documents listed on the accompanying Form PTO-1449 (4 sheets) for consideration by the Examiner in connection with the examination of the above-identified patent application.

Pursuant to 37 C.F.R. § 1.98 (a), the foreign patent and non-patent references listed on the attached Form PTO-1449 are enclosed. If it is determined that any of the listed references are not presently enclosed, the Examiner is requested to contact the undersigned so that a copy can be forwarded.

Applicants also respectfully advise the Examiner of the following co-pending U.S. Patent Applications which are commonly assigned to the owners of the instant application:

U.S. Application Serial No. 11/072,162, entitled "Tranexamic Acid Formulations", filed March 4, 2005, attached herewith as Exhibit A; and

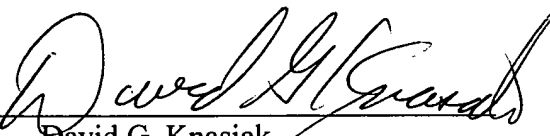
U.S. Application Serial No. 11/072,194, entitled "Tranexamic Acid Formulations", filed March 4, 2005, attached herewith as Exhibit B.

It is respectfully requested that the references cited in the accompanying Form PTO-1449 (5 sheets) and Exhibits A and B be considered and made of record.

This Information Disclosure Statement is filed under 37 C.F.R. § 1.97 (b), before the mailing of a first Office Action. Accordingly, no fee is believed due. In the event any fee is due in connection with the filing of this Information Disclosure Statement, the Commissioner is hereby authorized to charge said deficiency or credit overpayment to our Deposit Account No. 50-0552.

Respectfully submitted,

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FORM PTO-1449 (REV. 7-80)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTY. DOCKET NO.: 287.1006		SERIAL NO.: 10/631,371	
<b>LIST OF PRIOR ART CITED BY APPLICANT</b> (Use several sheets if necessary)				APPLICANT(S): RALPH A. HEASLEY, et al.			
				FILING DATE: July 31, 2003		GROUP: 1615	
U.S. PATENT DOCUMENTS							
*EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE	
CA							
FOREIGN PATENT DOCUMENTS							
DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION		
					YES	NO	
CB							
OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)							
CC	Pilbrant A, Schannong M, Vessman J., "Pharmacokinetics and bioavailability of tranexamic acid." <u>Eur J Clin Pharmacol</u> 1981;20:65-72.						
CD	Puigdemivol E, Carral M, Moreno J, et al., "Pharmacokinetics and absolute bioavailability of intramuscular tranexamic acid in man." <u>Int J Clin Pharmacol Therapy Toxicology</u> 1985;23:298-301.						
CE	Eriksson O, Kjellman H, Pilbrant A, et al., "Pharmacokinetics of tranexamic acid after intravenous administration to normal volunteers." <u>Eur J Clin Pharmacol</u> 1974;7:375-380.						
CF	Andersson I, Nilsson I, Colleen S, et al., "Role of urokinase and tissue activator in sustaining bleeding and the management thereof with EACA and AMCA." <u>Ann NY Acad Sci</u> 1968;146:642-658.						
CG	Dowd N, Karski J, Cheng D, et al. "Pharmacokinetics of Tranexamic Acid during Cardiopulmonary Bypass." <u>Anesthesiology</u> 2002;97:390-99.						
CH	Kaller H, "Enterale Resorption, Verteilung und Elimination von 4-Aminomethylcyclohexancarbonsäure (AMCHA) und a-Aminocaprinsäure (ACS) beim Menschen," <u>Naunyn-Schmiedeberg's Arch. Pharmacol. U. Exp Path.</u> 256: 160-169 (1967).						
CI	Andersson L, Eriksson O, Hedlund P, et al. "Special Considerations with Regard to the Dosage of Tranexamic Acid in Patients with Chronic Renal Diseases." <u>Urological Research</u> 6, 83-88 (1978).						
CJ	Nilsson I, "Clinical pharmacology of aminocaproic and tranexamic acids." <u>J Clin Pathol</u> , 33, Suppl (Roy Coll Path), 14, 41-47.						
CK	Melander B, Gliniecki G, Granstrand B, et al. "Biochemistry and Toxicology of Amikapron®; The Antifibrinolytically Active Isomer of AMCHA. (A comparative Study with e-Aminocaproic Acid)" <u>Acta pharmacol. et toxicol.</u> 1965, 22, 340-352.						
CL	Longstaff C, "Studies on the mechanisms of action of aprotinin and tranexamic acid as plasmin inhibitors and antifibrinolytic agents." <u>Blood Coagulation and Fibrinolysis</u> , 5, 537-542. (1994)						
CM	Dockeray C, Sheppard B, Daly L, et al., "The fibrinolytic enzyme system in normal menstruation and excessive uterine bleeding and the effect of tranexamic acid." <u>Eur. J. Obstet. Gynecol. Reprod. Biol.</u> , 24 (1987) 309-318.						
CN	Mohri H., "High Dose of Tranexamic Acid for Treatment of Severe Menorrhagia in patients with von Willebrand Disease." <u>Journal of Thrombosis and Thrombolysis</u> 14(3), 255-257, (2002).						
EXAMINER				DATE CONSIDERED			
*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.							

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	DA						
<b>FOREIGN PATENT DOCUMENTS</b>							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION
							YES NO
	DB						
<b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>							
	DC	Preston J, Cameron I, Adams E, et al. "Comparative study of tranexamic acid and norethisterone in the treatment of ovulatory menorrhagia." <u>British Journal of Obstetrics and Gynaecology</u> , May 1995, Vol. 102, pp. 401-406.					
	DD	Bonnar J, Sheppard B. "Treatment of menorrhagia during menstruation: randomized controlled trial of ethamsylate, mefenamic acid, and tranexamic acid." <u>British Medical Journal</u> 1996;313:579-82.					
	DE	Nilsson L, Rybo G. "Treatment of Menorrhagia with an Anti-fibrinolytic Agent, Tranexamic Acid (AMCA) A Double Blind Investigation." Nilsson, Lennart and Rybo, Göran, <u>Acta obst. Et gynec. scandinav.</u> 46, 572, (1967); 572-580					
	DF	Vermeylen J, Verhaegen-Declercq M, Verstraete M, et al. "A Double Blind Study of the Effect of Tranexamic Acid in Essential Menorrhagia." From the Laboratory of Coagulation-Proteolysis, Department of Medicine, University of Leuven, Belgium. 583-587.					
	DG	Callender S, Warner G, Cope E. "Treatment of Menorrhagia with Tranexamic Acid. A Double-blind Trial." <u>British Medical Journal</u> , 1970, 4, 214-216.					
	DH	Andersch B, Milsom I, Rybo G. "An Objective Evaluation of Flurbiprofen and Tranexamic Acid in the treatment of Idiopathic Menorrhagia." <u>Acta Obstet Gynecol Scand</u> 67:645-648, 1988.					
	DI	Milsom I, Andersson K, Andersch B, et al. "A comparison of flurbiprofen, tranexamic acid, and a levonorgestrel-releasing intrauterine contraceptive device in the treatment of idiopathic menorrhagia." <u>Am J Obstet Gynecol</u> 1991;164:879-83.					
	DJ	Gleeson N, Buggy F, Sheppard B, et al. "The effect of tranexamic acid on measured menstrual loss and endometrial fibrinolytic enzymes in dysfunctional uterine bleeding." <u>Acta Obstet Gynecol Scand</u> 1994; 73:274-277.					
	DK	Lee J, Hahn P, Van Dijk J, et al. "Treatment of Menorrhagia with Tranexamic Acid." <u>J Soc Obstet Gynaecol Can</u> 2000;22(10):794-8.					
	DL	Edlund M, Andersson K, Rybo G, et al., "Reduction of menstrual blood loss in women suffering from idiopathic menorrhagia with a novel antifibrinolytic drug (Kabi 2161)." <u>British Journal of Obstetrics and Gynaecology</u> 1995, Vol. 102, pp 913-917.					
	DM	Winkler U. "The effect of tranexamic acid on the quality of life of women with heavy menstrual bleeding." <u>European Journal of Obstetrics &amp; Gynecology and Reproductive Biology</u> 99 (2001) 238-243.					
	DN	Rybo G., "Tranexamic acid therapy – effective treatment in heavy menstrual bleeding. Clinical update on safety." <u>Therapeutic Advances</u> ISSN 0964-0673 Issue 4. (1991)					
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	EA	6	1	1	3	9	4	3	09/05/00	Okada et al.	424	457	
	EB	5	8	5	8	4	1	1	01/12/99	Nakagami et al.	424	489	
	EC	5	8	0	7	5	8	3	09/15/98	Kristensen et al.	424	489	
	ED	5	6	2	2	6	5	7	05/22/97	Takada et al.	264	4.32	
	EE	4	2	5	8	0	3	0	03/24/81	Sasaki et al.	424	94	
<b>FOREIGN PATENT DOCUMENTS</b>													
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												YES	NO
	EF												
<b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>													
	EG	Berntorp E. "No Increased Risk of Venous Thrombosis in Women Taking Tranexamic Acid." <u>Thromb Haemost</u> 2001; 86: 714-5.											
	EH	Bekassy Z, Astedt B. "Treatment with the Fibrinolytic Inhibitor Tranexamic Acid – Risk for Thrombosis?" <u>Acta Obstet Gynecol Scand</u> 1990; 69: 353-354.											
	EI	Mannucci P., "Hemostatic Drugs." <u>Drug Therapy</u> , Vol. 339, No. 4, p. 245-253 (1998).											
	EJ	Wellington K, Wagstaff A., "Tranexamic Acid – A Review of its Use in the Management of Menorrhagia." <u>Adis Drug Evaluation</u> , Drugs 2003;63(13):1417-1433.											
	EK	Dunn C, Goa K. "Tranexamic Acid – A Review of its Use in Surgery and Other Indications." <u>Adis Drug Evaluation</u> , Drugs 1999 Jun; 57 (6): 1005-1032.											
	EL	"An evidence-based guideline for the management of heavy menstrual bleeding. Working Party for Guidelines for the Management of Heavy Menstrual Bleeding." <u>NZ Med J</u> 1999; 112: 174-7.											
	EM	Lethaby A, Farquhar C, Cooke I. "Antifibrinolytics for heavy menstrual bleeding." <u>Cochrane Database of Syst Rev</u> 2002; (4).											
	EN	Lakhani K, Marsh M, Purcell W. "Uterine artery blood flow parameters in women with dysfunctional uterine bleeding and uterine fibroids: the effects of tranexamic acid." <u>Ultrasound Obstet Gynecol</u> 1998;11:283-285											
	EO	Ong, Y., et al., "Menorrhagia in von Willebrand disease successfully treated with single daily dose tranexamic acid." <u>Haemophilia</u> (1998), 4, 63-65											
	EP												
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	FA	4	4	8	3	8	6	7	11/20/84	Svahn et al.	424	279		
	FB	2004	00	0	6	0	2	1	01/08/04	Rojkjaer	514	12		
	FC													
	FD													
	FE													
	FF													
	FG													
<b>FOREIGN PATENT DOCUMENTS</b>														
		DOCUMENT NUMBER							DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
													YES	NO
	FH													
	FI													
	FJ													
<b>OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)</b>														
	FK	Walzman, M. and Bonnar, J., "Effects of Tranexamic Acid on the Coagulation and Fibrinolytic Systems in Pregnancy Complicated by Placental Bleeding", New Toxicology for Old Arch. Toxicol., Suppl. 5, 214-220 (1982).												
	FL	Cyclokapron® Package Insert. Pharmacia & Upjohn. Revised October 2000.												
	FM	Cyklokapron® Package Insert. Pharmacia Canada, Inc. Mississauga, Ontario. (Nov. 2002)												
	FN													
	FO													
	FP													
	FQ													
	FR													
	FS													
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